REMARKS

In the amendments herein, claim 4 has been amended. Claim 11 is new. Support for the amendments can be found in the application as filed, e.g., at page 26, line 10 – page 29, line 13, and Figure 4. Now pending in the application are claims 4 and 11.

No new matter has been added by these amendments.

The amendment of claims is without prejudice or disclaimer of the subject matter thereof and was done solely to expedite prosecution of the present application. Applicants reserve the right to pursue the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

Interview Summary

Applicants thank the Examiner for the courtesy of permitting a telephonic interview on August 12, 2008 ("the Interview"). During the Interview, the rejections of record were discussed. No final agreement was reached.

Priority Claim and Request for Corrected Filing Receipt

The present application is the U.S. national stage application under 35 USC §371 of PCT/JP03/00089, as correctly noted in the Official Filing Receipt dated 01/26/2006. However, Applicants note that certain records of the Patent Office (e.g., as viewed in PAIR) do not appear to reflect that the present application claims priority to Japanese application JP2002-005326, filed January 11, 2002. Applicants note with appreciation the Examiner's indication (in the Office Action) that the claim for priority has been acknowledged. Applicants respectfully request that a corrected filing receipt be issued reflecting this foreign priority claim, and that all Patent Office records be updated appropriately.

Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claim 4 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is traversed.

Claim 4 (as now pending) is directed to method of evaluating onset or onset possibility of rheumatoid arthritis in a human subject, the method comprising the steps of detecting whether a gene coding a protein comprising the amino acid sequence of SEQ. ID NO.:1 is present homozygously in the subject; and evaluating the onset or onset possibility of rheumatoid arthritis in the subject; wherein the homozygous presence of the gene in the subject is indicative of an increased possibility of onset of rheumatoid arthritis in the subject.

The Office Action discusses the Wands factors and states that claim 4 lacks enablement. Applicants do not agree with this analysis; some points are discussed in more detail below.

In the discussion of the Wands factors (at page 4 of the Office Action), the Office Action states that "the claims broadly encompass the absence of nt805 HOMO being predictive of the possibility of RA . . . it appears that the absence of detecting a gene that encodes SEQ ID NO1 is not predictably associated with the onset or possibility of onset of RA." This statement is traversed.

First, as discussed above, the pending claims are directed to a method in which, *inter alia*, the homozygous presence of the gene in the subject is indicative of an increased possibility of onset of rheumatoid arthritis in the subject. Thus, the claims does not recite that the absence of detecting a gene is predictably associated with the onset or possibility of onset of RA.

Further, as discussed previously and as shown in Figure 4 of the application, both in RA families and Sporadic families, the presence of the "nt805 homo" (homozygous 3-base-insertion mutation) genotype is associated with the development of RA. In fact, the nt805 homo genotype occurs only in the RA subjects. As noted previously, the Examiner stated (in the Office Action dated April 27, 2007) that "it appears that an association exists for humans homozygous for the presence of 'GGT' at position 805-807" (Office Action dated April 27, 2007, at page 5).

Moreover, Applicants provided additional data regarding this association in the "Declaration Under 37 CFR 1.132" (the "Declaration") filed September 11, 2007, demonstrating a statistical trend in that study group, as determined by the x^2 test.

Applicants further point out that the present claims are directed to a method of evaluating onset or onset possibility of rheumatoid arthritis in a human subject. Applicants contend that one of ordinary skill in the art would consider the presently-claimed method useful for evaluating onset or onset possibility of rheumatoid arthritis in a human subject, even if the correlation between the homozygous presence of the mutant gene and the development of RA is less than 100%. If desired, the present method could be used by a medical practitioner together with other diagnostic information to evaluate a subject's propensity for developing RA.

In view of the data presented in the subject specification, and in the Declaration, Applicants contend that one of ordinary skill in the art would be able to evaluate the onset or onset possibility of rheumatoid arthritis in a human subject by detecting whether a gene coding a protein comprising the amino acid sequence of SEQ. ID NO.:1 is present homozygously in the subject; and evaluating the onset or onset possibility of rheumatoid arthritis in the subject; wherein the homozygous presence of the gene in the subject is indicative of an increased possibility of onset of rheumatoid arthritis in the subject, as presently claimed.

The Office Action further discusses references (Hirschhorn et al. and Ioannides) that suggest that association studies are not reproducible. Applicants respectfully contend that no reason has been advanced to suggest that the studies presented in the present application and the Declaration are unreliable. To the contrary, as discussed herein, in addition to the data from the present application, an association between the homozygous presence of the mutant gene and the development of RA is seen in a study subsequent to the filing of the present application.

In the section titled "Response to Arguments", the Office Action states that the data provided in the specification and in the Declaration are "not consistent" and that "together the specification and the declaration suggest the mutation is unpredictable." These statements are traversed.

While the group studied as described in the Declaration is a group that includes many subjects having the homozygous 3-base-insertion mutation, as described above and in previous Responses, in both the study group discussed in the specification and in the study group discussed in the Declaration, the homozygous presence of the gene coding a protein comprising the amino acid sequence of SEQ. ID NO.:1 is associated with the tendency to develop RA. Applicants respectfully contend that any differences in the study populations do not call into question, and in fact confirm, that the pending claims are enabled.

Applicants respectfully contend that the specification provides enablement for the full scope of the pending claims, and, furthermore, that the claims meet all the requirements of, *inter alia*, 35 USC §112. Reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C. §102

Claim 4 stands rejected under 35 U.S.C. §102(b) as allegedly anticipated by Davis et al., PCT Patent Publication No. WO96/11269 (hereinafter, "the Davis publication"). This rejection is traversed.

Although the Office Action states that claim 4 "has a single active step of detecting SEQ ID NO 1 and the homozygosity and evaluation steps are conditional only upon the presence of homozygous detection," Applicants submit that this statement does not apply to the pending claims. Claim 4, as now pending, is directed to a method of evaluating onset or onset possibility of rheumatoid arthritis in a human subject, the method comprising the steps of: detecting whether a gene coding a protein comprising the amino acid sequence of SEQ. ID NO.:1 is present homozygously in the subject; and evaluating the onset or onset possibility of rheumatoid arthritis in the subject; wherein the homozygous presence of the gene in the subject is indicative of an increased possibility of onset of rheumatoid arthritis in the subject. Thus, the statement that "the homozygosity and evaluation steps are conditional only upon the presence of homozygous detection" does not apply to the pending claims (claim 11 being dependent on claim 4).

Applicants respectfully contend that the Davis publication does not teach or suggest that the homozygous presence in the subject of a gene as recited in claim 4 is indicative of an increased possibility of onset of rheumatoid arthritis in the subject. Therefore, Applicants contend that the Davis publication does not and cannot disclose a method of evaluating onset or onset possibility of rheumatoid arthritis in a human subject, and cannot anticipate the pending claims.

Claim 4 stands rejected under 35 U.S.C. §102(a) as allegedly anticipated by a publication of Shiozawa et al, Nippon Rinsho (2002) (hereinafter, "the Shiozawa publication"). This rejection is traversed.

Applicants note that the Shiozawa publication is, in pertinent part, the work of the present inventors published less than one year before the PCT filing date of the present application, and therefore is not available as prior art under 35 U.S.C. §102(a). Moreover, the present application claims the benefit of priority to application JP2002-005326, filed January 11, 2002 (prior to the publication date of the Shiozawa publication) (see above).

Applicants submit herewith a Declaration Under 37 C.F.R. 1.132 of the inventors, establishing that the Shiozawa publication is not available as prior art under 35 U.S.C. §102(a) (see, e.g., MPEP 716.10).

Reconsideration and withdrawal of the rejections is proper and the same is requested.

CONCLUSION

For at least the above reasons, Applicants contend that the application is in condition for allowance. Early and favorable consideration of the application is earnestly solicited.

Applicants conditionally request any extension of time necessary for this response to be considered timely filed. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith

(or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Reference No. 61646 (70904), Customer No. 21874.

Dated: August 14, 2008

Respectfully submitted,

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